Obesity and Chronic Pain
Systematic Review of Prevalence and Implications for Pain Practice

Samer Narouze, MD, PhD, and Dmitri Souzdalnitski, MD, PhD

Abstract: The combination of obesity and pain may worsen a patient's functional status and quality of life more than each condition in isolation. We systematically searched PubMed/MEDLINE and the Cochrane databases for all reports published on obesity and pain. The prevalence of combined obesity and pain was substantial. Good evidence shows that weight reduction can alleviate pain and diminish pain-related functional impairment. However, inadequate pain control can be a barrier to effective lifestyle modification and rehabilitation. This article examines specific pain management approaches for obese patients and reviews novel interventional techniques for treatment of obesity. The infrastructure for simultaneous treatment of obesity and pain already exists in pain medicine (eg, patient education, behavioral medicine approaches, physical rehabilitation, medications, and interventional treatment). Screening for obesity, pain-related disability, and behavioral disorders as well as monitoring of functional performance should become routine in pain medicine practices. Such an approach requires additional physician and staff training. Further research should focus on better understanding the interplay between these 2 very common conditions and the development of effective treatment strategies.

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Obesity is defined as an excess in body fat sufficient to affect health adversely.[1] Although not exactly reflecting fat mass, the body mass index (BMI) is commonly used as a marker of obesity. Obesity, defined by the World Health Organization (WHO) as a BMI of more than 30kg/m^2, affects more than 500,000 million adults worldwide, and overweight, defined as a BMI of 25 to 29.9 kg/m^2, affects more than 1.4 billion individuals.[2,3] According to the WHO, annually millions of people die of the consequences of obesity.

The prevalence of obesity has nearly doubled in the last 30 years.[4] In the United Kingdom, 25% of adults are obese, 64% are overweight, and more than 50% of all adults are predicted to develop obesity in the coming decades.[5] Although no significant changes in the prevalence of obesity in the United States were documented between 2003 and 2012, 16.9% of youth and 34.9% of adults are obese.[6]

Obesity increases the risk of cardiovascular disease, hypertension, and diabetes. Obesity also produces significant and well-recognized personal problems that are much more difficult to measure monetarily, such as social stigma, mood changes, decreased health-related quality of life (HRQL), and persistent pain.

The prevalence of chronic pain is comparable to the prevalence of obesity. Chronic pain affects about one-third of the population, both worldwide[7] and in the United States.[8]

From the Center for Pain Management, Western Reserve Hospital, Cuyahoga Falls, OH.
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Address correspondence to: Samer Narouze, MD, PhD, Western Reserve Hospital, 1900 23RD Street, Cuyahoga Falls, OH 44233 (e-mail: narouzs@hotmail.com).
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A number of articles published over the last few decades have examined the relationship of obesity and chronic pain. Although older studies did not substantiate a link,[9,10] recent and larger studies point toward a possible association between obesity and pain. One study showed that almost 40% of obese individuals suffered from chronic pain, with the prevalence increasing proportionally with BMI, and 90% of the study participants reported moderate to severe pain.[11] Another large survey of more than 1 million individuals (n = 1,062,271) showed that overweight individuals had about 20% more pain compared with normal-weight people, obese individuals with BMIs of 30 to 34 kg/m^2 had about 68% more pain, those with BMIs of 35 to 39 kg/m^2 had 136% more pain, and those whose BMIs were more than 40 kg/m^2 reported having 254% more pain.[12] A study of more than 3000 twins showed that after adjusting for age, sex, and the presence of depression, overweight and obese twins were more likely to report chronic widespread pain, low-back pain, tension-type or migraine headaches, abdominal pain, and fibromyalgia than the control group of normal-weight twins.[13]

The combination of obesity and pain worsens HRQL more substantially than either condition alone; the HRQL and family and local lives of obese subjects are affected; and higher BMI corresponds to worse impairment and worse pain.[11,14] Chronic pain increases the already huge societal burden of obesity in terms of Social Security and the financial burden of disability and health care costs.[15] In addition to final organ damage, the increase in fat mass of obese individuals facilitates the development of a range of incapacitating musculoskeletal conditions. Concordantly, chronic pain is an essential mediator of the effects of an increased BMI on HRQL in numerous conditions, including many degenerative and inflammatory musculoskeletal disorders, painful diabetic neuropathy, and headaches.[8]

As an example, obese patients require joint replacement surgeries at younger ages because of osteoarthritis (OA). Obese patients who were candidates for these surgeries had a higher frequency of intractable pain episodes than did nonobese patients.[16] The pain led to greater interference with sleep, walking distance, and social relations. In addition, obese patients more commonly used strong opioids and high doses of nonsteroidal anti-inflammatory drugs.[16] Finally, surgeries on obese patients are associated with perioperative challenges for adequate pain control, which slows rehabilitation and often results in persistent pain.[8] Some have hypothesized that effective weight reduction can decrease the burden of obesity comorbidities, including chronic pain.[17] Pain physicians not only should be familiar with these strategies but also should use them efficiently for their patients.

Evidence-based studies of obesity and chronic pain are restricted to specific specialties such as rheumatology[18–21] or to specific conditions such as arthritis[22–24] and low-back pain. Only a limited number of articles on this topic have been published in pain medicine literature. These include expert opinions and narrative reviews,[25–29] some cross-sectional and retrospective studies,[12,13,30–40] 1 randomized controlled trial (RCT),[41] reviews, and some others. To the best of our knowledge, there are no systematic analyses of relevant prevalence studies of pain in the obese population or pertinent calls for action in pain medicine. In addition, the substantial

number of very recent studies shedding light on the association of obesity and pain requires a systematic review.

The information presented in this article emphasizes recent developments and highlights the potentially important role that pain medicine physicians may play in simultaneous weight reduction and chronic pain management for obese patients.

METHODS

We systematically searched PubMed/MEDLINE and the Cochrane databases for all reports published in any language between the earliest available date (the first publication in the PubMed/MEDLINE dated 1949) and September (third week) 2014 using the following key words: *obesity*, *pain*, and *body mass index*. We used the WHO definition of obesity,[2] placed no language restrictions, and limited the search to human subjects. The following is an example of the primary query performed for the PubMed/MEDLINE database: ("pain" [MeSH Terms] OR "pain" [All Fields]) AND ("obesity" [MeSH Terms] OR "obesity" [All Fields]). The supplemental query included BMI and pain: (BMI [All Fields] AND ("pain" [MeSH Terms] OR "pain" [All Fields]). We searched primarily for evidence-based publications, including systematic reviews, meta-analyses, large longitudinal cohort studies, and RCTs. If high-level (1A, B and 2A, B)[42] evidence-based studies were not available, we included original articles with small cohorts, case-control or cross-sectional designs, and other clinical trials.

We undertook a further step in filtering to exclude nonrelevant articles via titles and abstracts. If no systematic reviews were uncovered on the specific pain conditions known to be related to obesity, we further searched both databases for the association of other keywords such as obesity and back, upper or lower extremity (including shoulder, hip, knee, and foot), headache disorders (including migraine and tension headaches), neuropathic pain, and other relevant terms. After reviewing summaries of the articles, we obtained full-text articles where appropriate. We used relevant systematic reviews, meta-analyses, clinical trials, and high-quality observational studies in this review. While systematically reviewing the prevalence of pain in obese patients and the prevalence of increased BMI in patients with chronic pain, we excluded narrative reviews, case reports, letters, editorials, and guidelines. We categorized the level of evidence for treatment efficacy or the relationship between obesity and chronic pain conditions and sorted relevant recommendations of the studies chosen for the review according to Guyatt et al[42] (Table 1). This approach to classifying the evidence considers the study type (systematic review, meta-analysis, RCT, or other clinical study) and quality (methodological design such as sample size and power analysis). We categorized the level of evidence of systematic reviews or meta-analyses by the quality and quantity of the studies incorporated into each systematic review or meta-analysis. Both of the authors (S.N. and D.S.) independently performed the search and extracted data from articles, with incongruities resolved by debate.

Search Results

The primary query yielded 4225 records, of which 118 were systematic reviews (17 with meta-analysis), and 428 were clinical trials and observational studies. The supplemental query yielded 2413 records that included 41 systematic reviews (10 with meta-analysis), 381 clinical trials, and observational studies. The Cochrane database search identified 10 systematic review records on the primary query and 4 in the supplemental query. The collected literature focused on the association of obesity and chronic pain (Fig. 1). We found no evidence-based publications on the role of the pain physician in the treatment of an obese patient with persistent pain other than articles on perioperative management of obese patients and 1 article on interventional treatment. Therefore, we analyzed available literature in the following areas: (1) prevalence of pain in obese patients and prevalence of chronic pain in obese

TABLE 1. Levels of Evidence and Recommendations

Grade of Recommendation/ Description	Benefits vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
1A/strong recommendation, high-quality evidence	Benefits clearly overweigh risk and burdens, or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B/strong recommendation, moderate-quality evidence	Benefits clearly overweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C/strong recommendation, low- or very low-quality evidence	Benefits clearly overweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation, but may change when stronger evidence becomes available
2A/weak recommendation, high-quality evidence	Benefits closely balanced with risk and burdens	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on patients' or societal values
2B/weak recommendation, moderate-quality evidence	Benefits closely balanced with risk and burdens	RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on patients' or societal values
2C/weak recommendation, low-quality or very low-quality evidence	Uncertainty in the estimates, benefits, risk, and burden; benefits, risk, and burden may be closely balanced	Observational studies or case series	Very weak recommendation, other alternatives may be equally reasonable

Adapted with permission from Guyatt et al.[42]

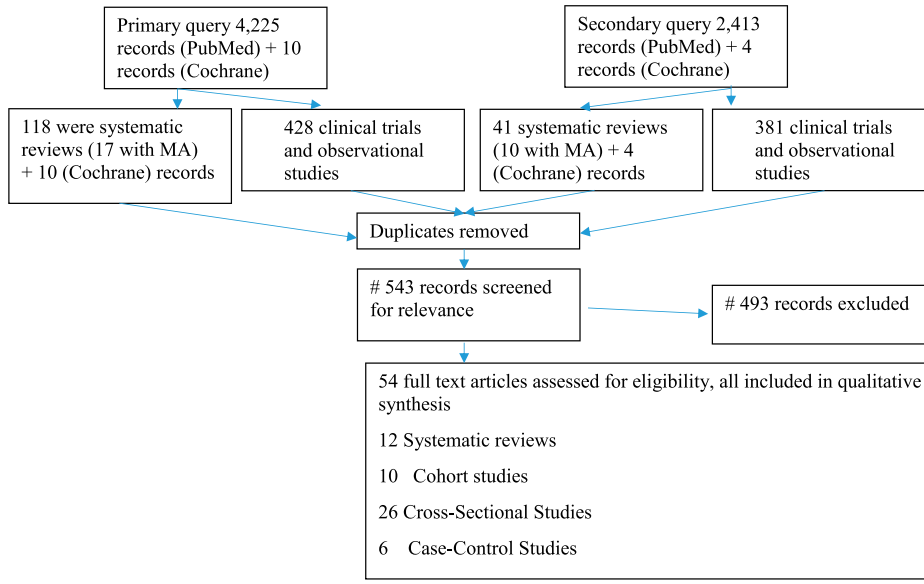

FIGURE 1. PRISMA flow diagram.

patients (in a systematic review fashion), (2) mechanisms of association of obesity and pain (narrative review), and (3) implications for pain medicine practice (narrative review). The narrative review for the analysis of mechanisms of association of obesity and pain was mandated by the enormous number of experimental and basic science studies, which are beyond the scope of this primarily clinical review. The discussion of implications for pain practice is based predominantly on evidence-based publications but not in strictly systematic fashion because the need to cover a broad array of topics, including physical, behavioral, pharmacological, interventional, and perioperative treatment, would have prevented publication in the limited space allocated for this article.

Because of the substantial number of articles on the prevalence of obesity and pain, we organized presentation of the available data by patient complaints (eg, back pain, upper- and lower-extremity pain, headaches) rather than by specific pathologic conditions (eg, OA, rheumatoid arthritis [RA], migraine). The review progresses by level of evidence, starting with systematic reviews and meta-analyses and initially describing obesity and spine pain and obesity and OA, the most commonly described associations. The interrater agreement was 83%, $\kappa = 0.667 \pm 0.07$ (95% confidence interval, 0.53–0.80). One limitation of the search is that most of the discovered epidemiologic studies used BMI as the sole indicator of obesity without considering other syndromes also recognized as obesity, such as normal-weight obesity (elevated body fat percentage) and metabolic obesity, which is characterized by increased waist circumference, fasting blood glucose and triglycerides values, hypertension, and reduced high-density lipoprotein cholesterol values.[43]

DISCUSSION

Prevalence of Pain in Obese Individuals

Back and Radicular Pain

Although results of older studies were not conclusive about the relationship between obesity and back pain,[9,10] the recent higher-quality studies showed a strong association between low-back pain with or without radicular symptoms and obesity. One systematic review of 95 studies, which included a meta-analysis of 33 studies, confirmed the association between overweight/obesity and increased prevalence of low-back pain in the past 12 months (pooled odds ratio [OR], 1.33), seeking care for low-back pain (OR, 1.56), and chronic low-back pain (OR, 1.43).[44] Obese subjects had a higher prevalence of low-back pain compared with those who were overweight, and overweight individuals had a higher prevalence of low-back pain than did people of normal weight (both groups, n = 102,943). Overweight and obesity were strongly associated with seeking care for acute and chronic low-back pain.

Another recent systematic review and meta-analysis examined 26 studies, with a sample size of up to 73,982 individuals.[45] Both overweight (OR, 1.23) and obesity (OR, 1.40) were associated with lumbar and radicular pain in men and women, with a dose-response relationship. Overweight (OR, 1.16) and obesity (OR, 1.38) in this study were associated with an increased risk of hospitalization for sciatica, and both were associated with an increased risk of surgery for lumbar disk herniation (OR, 1.89). Obesity also has been cited as a risk factor for the first-time incidence of sciatica.[46] Researchers of this systematic review stressed that obesity is a modifiable risk factor for sciatica.

One cross-sectional Austrian study (n = 178,818) found that the age-standardized prevalence of back pain was 32.9%, but that the prevalence was significantly higher among women than men and in obese than nonobese subjects.[47] Obese men showed the uppermost increase in and greatest risk for back pain. Interestingly, 2 other large European studies, involving 105,841 participants in Norway and the Netherlands, found that the association of higher BMI with back pain was stronger in women.[48,49] One systematic review confirmed that obese women are at high risk for a variety of musculoskeletal problems, primarily back pain.[50] Another cross-sectional study involving 2510 individuals found that BMI, age, and depression independently predicted disabling chronic low-back pain compared with persons without pain.[32] However, BMI was eliminated when predicting disabling chronic low-back pain compared with persons with nondisabling chronic low-back pain; age, widespread pain, and depression independently predicted disabling chronic low-back pain.

A cross-sectional study revealed an association between obesity, measured by evidence of outer abdominal fat, and lumbar facet OA on computed tomography scans.[51] A recent large cross-sectional study from Spain involving 43,072 participants found that obesity was associated not only with low-back pain, but also with

neck pain.[52] Another investigation demonstrated that greater adipose tissue, but not lean overall tissue mass, was linked to both higher intensity of low-back pain and higher disability levels.[53]

Upper- and Lower-Extremity Pain

The association of obesity with pain in the arms and legs, especially OA, is 1 of the major themes in clinical literature.[54] More than two-thirds of patients with painful OA were overweight or obese in 1 Italian study.[55] More intense pain in obese individuals was associated with the presence of comorbidities and a lower level of education. Obesity was a significant risk factor for pain in all OA localizations, including knee, hip, and generalized OA. A systematic review demonstrated that the risk for knee OA was 7 times greater for obese individuals than for individuals with normal weight, with ORs ranging from 2.8 to 7.48 and a relative risk of up to 8.1.[56] A cross-sectional study showed that the ORs for both OA and inflammatory arthritis were up to 7 times higher for obese people compared with those categorized as normal weight or underweight.[57] Obese people reported more pain (for hip arthritis, hip OA, and knee OA), more stiffness (for hip arthritis, knee arthritis, and knee OA), greater disease severity (all diagnoses), decreased HRQL (for hip arthritis and hip OA), and worse function (all conditions).

In another recent study, mobility, mobility-related self-efficacy, and pain related to knee OA were found to be functions of the severity of obesity.[58] One case-control study showed that not only was an increased BMI associated with knee and hip OA, but also those who became overweight earlier in their adult lives demonstrated higher risks of lower-extremity OA.[59] The deteriorative effect of increased BMI on pain and self-reported disability was observed up to end-stage OA.[60] A small (n = 112) but well-conducted cohort study found that even a small weight gain was associated with accelerated knee cartilage volume loss and worsened pain.[61] Conversely, and importantly, even a small weight loss was associated with reduced knee cartilage volume loss and less pain.

Being overweight at the time of the diagnosis of RA significantly decreases the probability of attaining good disease control during the early phase of RA.[62] Only narrative reports address the association of obesity and gout, another metabolic disease. The association was attributed primarily to shared metabolic abnormalities between these 2 conditions.[63]

A systematic review of 25 articles about BMI and foot disorders showed a strong association between overweight/obesity and overall foot pain and specifically with chronic plantar heel pain (in nonathletic people).[64] Evidence was inconclusive for an association with hallux valgus, tendonitis, foot OA, and flat foot. Incident foot pain in overweight subjects has been associated with fat mass rather than solely BMI.[65] Obesity, specifically android ("apple") fat mass, was strongly associated with foot pain; gynoid ("pear") fat mass was inversely related to foot pain. Skeletal muscle mass was not associated with foot pain.[66] Conversely, patellar tendinopathy was related to BMI but not to the fat mass. The difference was explained by a mechanical pathogenesis of patellar tendinopathy.[67] According to a recent systematic review, good evidence supports obesity as an overall risk factor for tendinopathy.[68] Upper-extremity pain is a common complaint contributing to decreased HRQL, an important cause of occupational disability, and a substantial contributor to health care spending. The prevalence of general shoulder pain during the preceding 30 days is between 16% and 31%.[69] Two systematic reviews showed that abnormal BMI was strongly associated with an increased incidence of shoulder pain.[69,70] Shoulder pain was associated with an increased BMI, waist circumference, and waist-to-hip ratio in both sexes and metabolic syndrome only in men.[71] Investigators showed a 2.8% prevalence of chronic rotator cuff tendinopathy that was associated with waist circumference only in men. Vehmas and colleagues[40] evaluated a cohort of patients with wrist tenosynovitis, carpal tunnel syndrome or ulnar nerve entrapment, elbow epicondylitis, and shoulder or other upper-extremity pain. They found a strong link between visceral fat thickness and pain intensity that was more prominent than other obesity variables, including waist circumference. Obese individuals in another investigation were at more significant risk than their normal-weight counterparts for severity and occurrence of rotator cuff tears.[72]

Chronic Widespread Pain and Fibromyalgia

Chronic widespread pain affects more than 17% of the general population, according to an 11-year prospective study in Europe involving 28,367 individuals.[73] Investigators also showed that chronic widespread pain is closely associated with overweight and obesity. This association was confirmed in a recent Korean study, which showed that an increase in adipose tissue mass and adipose tissue mass/muscle ratio was associated with musculoskeletal pain among women.[74] A cohort study of 385 female Finnish kitchen workers, evaluated repeatedly at 3-month intervals over 2 years,[75] documented an increased prevalence of widespread pain (OR, 2.8) associated with obesity. Conversely, not being obese was associated with a reduced prevalence of widespread pain (OR, 3.7), defined in this study as hurting at 3 or more of 7 sites.

Obesity was extremely prevalent in patients with fibromyalgia in another cross-sectional study of 215 women, with about 80% of patients who had fibromyalgia being obese or overweight.[36] Obesity in fibromyalgia was associated with greater pain sensitivity, worse sleep quality, and reduced physical capacities.[36,76]

Headaches

The general association between obesity and headache is well documented. Obese patients have been shown to be much more likely to have or to have progressed to chronic daily headaches than patients with BMIs less than 25 (ORs, 1.34 and 5.28, respectively).[77] This association was more robust in those with chronic headaches compared with episodic headaches in another large analysis encompassing more than 200,000 adults.[78] Obese individuals not only were more likely to suffer from headaches than nonobese subjects, but the risk of headaches rose proportionally with an increase in BMI; the highest risk was seen in morbidly obese individuals.

A recent systematic review showed that among specific primary headaches, the association of migraine headaches and obesity was most prominent and, in most studies, statistically significant ($P < 0.001$) for both episodic and chronic (>15 d/mo) migraines.[79] Although the authors of this review concluded that there was no correlation between obesity and migraine frequency, a more recent cross-sectional study stated that this relationship is likely.[80] Interestingly, patients with a history of migraine headaches were slightly more likely to become overweight or obese.[81] A higher BMI, but not the abdominal obesity, was associated with migraines in adults in another study.[82] Obesity commonly accompanies chronic daily headaches and is considered a significant risk factor for transforming episodic migraines to chronic.[83] Finally, individuals with proven insulin resistance had almost 4 times the odds of having chronic migraines compared with unaffected individuals.[84]

Chai and colleagues[79] reported in their systematic review that the link between tension-type headache, the most common headache disorder, is established in some studies but is considered to be controversial in others.

Among secondary headaches (disorders with a well-defined cause of the headache), idiopathic intracranial hypertension, also

known as pseudotumor cerebri, is most commonly mentioned in the literature as associated with obesity.[79] This classically occurs in obese women but is also described in men. Idiopathic intracranial hypertension is characterized by a progressive headache associated with increased cerebrospinal fluid pressure, visual field deficits, papilledema, and sometimes sixth nerve palsies. Headaches are reported by almost all affected patients and are typically the earliest sign of the disease. Abdominal adiposity also is common in these patients.[79]

Abdominal and Pelvic Pain

Eslick found a significant association of upper abdominal pain with increased BMI (OR, 2.65)[85] but no significant associations for general abdominal pain or lower abdominal pain. Two small cross-sectional studies involving 91 women[86] and 250 men[87] showed an association between obesity and pelvic pain in both sexes. Dysmenorrhea, a common menstrual complaint seen in 16% to 91% of women of reproductive age that causes severe pain in 2% to 29%, was not associated with obesity.[88]

Chronic Neuropathic Pain

Obesity was 1 of the comorbidities of chronic neuropathic pain in a cross-sectional study examining 3011 people.[89] One case-control study demonstrated that obese individuals had subclinical impairment of nerve function, represented by significantly altered compound muscle action potential amplitude in some lower-extremity nerves and decreased sensory action potential amplitude and impaired sensory thresholds of all examined nerves.[90] Small-fiber neuropathy, a very common but not well-understood condition, was present in obese patients before the development of pain and in individuals with or without hyperglycemia and hyperinsulinemia.[91] Other investigators evaluated 100 patients with diabetic neuropathy after excluding all persons who had mobility limitations.[92] Impaired functional capacity was related to decreased muscle strength and BMI but not to neuropathy.

In addition to general painful neuropathy, local neuropathic conditions are associated with obesity. The risk of developing meralgia paresthetica was doubled in obese patients.[93] A case-control study of 600 patients found obesity to be an independent risk factor for median neuropathy that presented clinically as carpal tunnel syndrome.[94]

Obesity and Pain in Children and Elderly

A recent systematic analysis of musculoskeletal pain complaints in children 3 to 18 years of age reviewed 11 studies.[95] Increased BMI had a significant (in most studies $P < 0.001$) impact on the children's pain reporting, physical health, exercise, and HRQL. Bone deformity and dysfunction in association with chronic musculoskeletal pain and obesity were frequently reported findings. A longitudinal study evaluated 3376 adolescents for the association of obesity and pain.[96] The mean age was 17.8 years, and 7% of study participants were obese. Obese adolescents were more likely to report musculoskeletal pain, especially knee pain and chronic regional pain, had higher pain scores, and potentially had worse prognoses. Investigators also have reported an overlay between increased BMI and headaches in children.[97]

The association between pain and obesity in elderly individuals is discussed in the literature primarily in the form of narrative review.[98] One study showed that elderly obese individuals (≥70 years, n = 736) had both greater functional disability and an increase in the number of people reporting pain. Pain was a significant mediator of the adverse effects of obesity on physical function in older women but not in men. A study of 2629 individuals older than 65 years in Taiwan documented the impact of obesity and sarcopenia (change in muscle structure and performance associated with aging) on patients' physical performance but not on pain.[99] Of 407 New York residents 70 years or older, 52% had chronic pain, [35] and central obesity was significantly associated with pain (OR, 2.03). After adjusting for inflammation measured with C-reactive protein, insulin resistance, and pain-interrelated comorbidities, central obesity predicted higher pain scores and almost doubled the risk of persistent pain (OR, 1.70). The authors could not explain the relationship between obesity and chronic pain by biomechanical factors, neuropathy, or markers of insulin resistance or inflammation alone.[35]

Mechanisms of the Obesity and Chronic Pain Relationship

Identifying the mechanisms of the relationship between obesity and chronic pain can allow clinicians to better serve the needs of affected patients. The following possible causations are discussed in the literature: (1) Obesity is a risk factor for chronic pain, (2) Chronic pain is a risk factor for obesity, and (3) obesity and chronic pain are comorbid conditions. Comorbidity denotes a greater than coincidental association of distinct conditions in the same subject.[100] A fundamental causal relationship between obesity and pain remains the subject of debate. A good body of evidence (Table 2) suggests that obesity is a risk factor both for general chronic pain and for specific nosologies. On the other hand, a reverse option suggesting that pain is a risk factor for obesity also is conceivable because many people experiencing persistent pain, with or without a history of preceding injury, reduce their physical activity levels, leading to more deconditioning and eventually more pain.[25,29] The "comorbidities" option also appears to be viable because a variety of factors, such as behavioral idiosyncrasies, smoking status, dietary habits, physical activity pattern, overall health status, or individual history, all may contribute to the pathophysiologic pathways of both obesity and chronic pain. Individual history (gaining weight in early adulthood) and biomechanical and structural factors are believed to play the primary role in the development of coexisting obesity and pain.[101,102] On a population level, however, these factors could not explain an interplay between obesity and pain. For example, in a study involving more than 1 million people, obesity continued to be linked to persistent pain even when accounting for the effects of a variety of health problems and conditions known to produce pain.[12] Therefore, the mechanisms of the obesity and pain relationship are likely multifactorial and involve the interactions of genetic, metabolic, biomechanical, environmental, behavioral, social, and cultural factors.[13,25,29,103]

Genetic Mechanisms

A growing body of data suggests the magnitude of inherited factors for obesity.[1] Pain in obese individuals also has been highly associated with genetic factors. For example, the heritability effects of low-back pain in a systematic review of 27 twin studies ranged from 21% to 67% and were strongly associated with both pain and obesity.[104] In addition, depression and some other conditions share a genetic risk with obesity.[105] An increasing number of basic science and clinical publications have examined specific genes contributing to both problems. For example, the long-known link between the aggrecan gene variable number of tandem repeats polymorphism and intervertebral disk degeneration[106] recently was shown to be associated with obesity in painful lumbar disk herniation.[107]

Heterozygous mutations in melanocortin receptor 4 (MC4R) is a common genetic form of severe obesity. This receptor protein is encoded in humans by the *MC4R* gene, which is abnormal in 2% to 3% of obese children and up to 5% of patients with severe early-onset obesity.[1]

TABLE 2. Evidence Supporting Obesity as a Risk Factor for the Development of Chronic Pain and Chronic Pain as a Comorbidity of Obesity

Condition	Level of Evidence	Source	Type of Study	Cohort or Sample Size	Comments
Overall pain	1A	Stone et al,[12] 2012	Cross-sectional study	n = 1,062,271	• Overweight individuals had about 20% more pain compared with normal-weight individuals.
					• Obese subjects with BMI 30–34 kg/m^2 had about 68% more pain.
					• Obese subjects with BMI 35–39 kg/m^2 had 136% more pain.
					• Obese subjects with BMI >40 kg/m^2 reported having 254% more pain.
	1A	Wright et al,[13] 2010	Cross-sectional twins study	n = 3471	• After adjusting for age, sex, and depression, overweight and obese twins were more likely to report chronic widespread pain, low-back pain, tension-type or migraine headaches, abdominal pain, and fibromyalgia than the control group of twins.
Back pain and radicular pain					
Low-back pain with radicular symptoms	1A	Shiri et al,[45] 2014	Systematic review and meta-analysis	n = 19	• Both overweight (OR, 1.23) and obesity (OR, 1.40) (n = 19,165) were associated with lumbar radicular pain, and sciatica in men and women, with a dose–response relationship.
				26 Studies (8 cross-sectional	• Overweight (OR, 1.16) and obesity (OR, 1.38) were associated with increased risk of hospitalization for sciatica.
					• Overweight/obesity was associated with increased risk of surgery for lumbar disk herniation (OR, 1.89; n = 73,982).
Low-back pain	2B	Leboeuf-Y de,[9] 2000	Systematic review	n = Not defined	• About 1/3 of all studies discovered a statistically significant positive weak association between increased weight and lower back pain.
				65 Studies	• 2B level of evidence because the extraction/review was carried out by only one author.
	1A	Leboeuf-Y de et al,[10] 1999	Cross-sectional twins study	n = 29,424	• Obesity was associated with low-back pain, particularly with chronic or recurrent low-back pain. The association was weak but unlikely causal.
	1B	Heuch et al,[48] 2010	Cross-sectional study	n = 92,936	• The prevalence of persistent low-back pain was higher among subjects with increased BMI.
					• The association was stronger in women.
	1C	Häuser et al,[32] 2014	Cross-sectional study	n = 2510	• Age, BMI, and depression independently predicted disabling chronic low-back pain compared with persons without pain.
					• Age, widespread pain, and depression independently predicted disabling chronic low-back pain compared with persons with nondisabling chronic low-back pain.
Radicular symptoms only	1B	Cook et al,[46] 2014	Systematic review	n = 78,856	• Risk factors for sciatica included obesity.
				8 Studies	• Obesity was suggested to be 1 of the modifiable risk factors.
Seeking care for low-back pain	1A	Shiri et al,[44] 2010	Systematic review	n = See comments 95 studies in systematic review, 33 studies in meta-analysis	• There was a strong association between overweight/obesity and increased prevalence of low-back pain in the previous 12 mo (OR, 1.33; n = 102,943), seeking care for low-back pain (OR, 1.56; n = 147,243), and chronic low-back pain (OR, 1.43; n = 64,226).

Back pain unspecified	1B	Großschädl et al,[47] 2014	Cross-sectional study	n = 178,818	• The age-standardized prevalence of back pain was significantly higher in obese than nonobese subjects. • Obese men showed the uppermost increase of and greatest risk for back pain.
Lumbar facet OA	1B	Jentzsch et al,[51] 2014	Case-control study	n = 629	• Obesity measured as outer abdominal fat was associated with lumbar facet OA.
Both upper and low-back pain	1B	Palacios-Ceña et al,[52] 2014	Cross-sectional study	n = 43,072	• Both neck pain and low-back pain were associated with obesity.
Low-back pain and disability	1C	Urquhart et al,[53] 2011	Cross-sectional study	n = 135	• Greater fat, but not lean tissue mass, was linked to higher intensity of low-back pain and higher disability levels.
Extremity pain					
Pain associated with OA overall	1B	Cimmino et al,[55] 2013	Cross-sectional study	n = 26,896	• 2/3 of patients with symptomatic OA were overweight or obese. • Obesity was clearly associated with all OA locations, knee > hip > hand.
Knee OA	1A	Lee and Kean,[56] 2012	Systematic review and meta-analysis	n = 176	• The risk for knee OA was 7 times greater for obese individuals compared with those with normal weight • The OR ranged, depending on the study, from 2.8 to 7.48, with a relative risk of up to 8.1.
OA and inflammatory arthritis	1B	Ackerman and Osborne,[57] 2012	Cross-sectional study	n = 1157	• The odds of arthritis and OA was up to 7 times higher for obese subjects compared with those categorized as being normal weight or underweight. • Obese subjects reported more pain (hip arthritis, hip OA, and knee OA), more stiffness (for hip arthritis, knee arthritis, and knee OA), greater disease severity (all diagnoses), decreased HRQL (for hip arthritis and hip OA), and worse function (all conditions).
RA	1A	Sandberg et al,[62] 2014	Cohort study	n = 495	• Being overweight at the time of the diagnosis of RA significantly decreased the probability of attaining good RA control during the early phase of the disease.
Knee and hip OA	1C	Holliday et al,[59] 2011	Case-control study	n = 3,170	• Increased BMI was associated with knee and hip OA. • Adults who became overweight earlier demonstrated higher risks of lower-extremity OA.
Knee OA	1B	Garver et al,[58] 2014	Cross-sectional study	n = 174	• Mobility, determined with an accelerometer, and pain related to knee OA were found to be a function of the severity of obesity.
	1C	Kauppila et al,[60] 2009	Cross-sectional study	n = 88	• The deteriorative effect of an increased BMI on pain and self-reported disability was observed up to the end stage of OA.
	1A	Teichtahl et al,[61] 2014	Cohort study	n = 112	• Even a small weight loss was associated with reduced knee cartilage volume loss and less pain. • Weight gain was associated with accelerated knee cartilage volume loss and worsened pain.

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TABLE 2. *(Continued)*

Condition	Level of Evidence	Source	Type of Study	Cohort or Sample Size	Comments
Foot pain	1A (foot pain overall) 2C (foot OA)	Butterworth et al,[64] 2012	Systematic review	n = Not defined 25 Studies	• There was a strong association between overweight/obesity and foot pain overall and chronic plantar heel pain specifically in nonathletic people. • The evidence was inconclusive for an association with hallux valgus, tendonitis, foot OA, and flat foot. • Some limited evidence supported weight loss to reduce foot pain.
	1B	Butterworth et al,[65] 2013	Cohort study	n = 51	• Incident foot pain in overweight subjects was associated with fat mass rather than only BMI.
	1B (foot pain) 1C (skeletal mass)	Tanamas et al,[66] 2012	Cross-sectional study	n = 136	• Obesity, specifically android ("apple") fat mass, was strongly associated with foot pain. • Gynoid ("pear") fat mass was inversely related to foot pain. • Skeletal muscle mass was not associated with foot pain.
Patellar tendinopathy	1B	Fairley et al,[67] 2014	Cross-sectional study	n = 297	• Patellar tendinopathy was related to BMI but not to fat mass.
Tendinopathy	1A (tendinopathy in general) 1C (specific tendinopathy)	Franceschi,[68] 2014	Systematic review	n = 44,828 15 Studies	• Obesity was a risk factor for overall tendinopathy. • An exact degree of the impact of obesity was not well defined for specific tendinopathy.
Shoulder pain	1C	Viikari-Juntura et al,[70] 2008	Systematic review	n = 30,146 14 Studies	• Heterogenic studies, therefore 1C. • Abnormal BMI was associated with an increased incidence of shoulder pain in 4 studies examining this relationship.
Shoulder pain and rotator cuff tendinopathy	1B	Rechardt et al,[71] 2010	Cross-sectional study	n = 6237	• Shoulder pain was associated with increased BMI, waist circumference, and waist • Chronic rotator cuff tendinopathy was associated with weight
Rotator cuff tears	1C	Gumina et al,[72] 2014	Cross-sectional study	n = 381	• Obesity was a significant risk factor for the occurrence and severity of rotator cuff tears.
Upper-extremity pain	1B	Vehmas et al,[40] 2013	Cohort study	n = 177	• Visceral fat thickness was strongly associated with pain intensity in patients with wrist tenosynovitis, carpal tunnel syndrome or ulnar nerve entrapment, elbow epicondylitis, and shoulder or other upper-extremity pain.
Other musculoskeletal problems					
Chronic widespread pain	1A	Mundal et al,[73] 2014	Cohort study	n = 28,367	• Chronic widespread pain was closely associated with overweight and obesity.
	1B	Haukka et al,[75] 2012	Cohort study	n = 385	• Obesity was associated with an increased prevalence of widespread pain (OR, 2.8). • Not being obese was associated with a reduced (OR, 3.7) prevalence of widespread pain, which was defined as hurting at ≥3 of 7 sites.

Fibromyalgia	1B	de Araújo et al,[76] 2014	Cohort study	n = 100	• Women with symptomatic obstructive sleep apnea showed greater weight gain after the diagnosis of fibromyalgia when compared with controls (11.7 and 6.4 kg, respectively, $P < 0.05$).
	1C	Okifuji et al,[36] 2010	Cross-sectional study	n = 215	• Obesity was a prevalent comorbidity of fibromyalgia and may contribute to fibromyalgia severity. • About 80% of patients with fibromyalgia were obese or overweight. • Obesity in fibromyalgia was associated with greater pain sensitivity, worse sleep quality, and reduced physical capacities. • Weight management should possibly be incorporated into treatment.
Musculoskeletal pain	1C	Yoo et al,[74] 2014	Cross-sectional study	n = 1530	• Increase in adipose tissue mass and adipose tissue mass/muscle ratio was considerably associated with musculoskeletal pain among women. • Widespread pain was significantly associated with a high fat/muscle ratio after adjusting for confounders.
Headaches					
Migraine, TTH, IIH	1A (headaches in general) 1A (migraines) 1C (TTH) 1A (IHH)	Chai et al,[79] 2014	Systematic review	n = Not specified 16 studies	• The risk of headaches was increased in the obese, with risk increasing with higher BMI. This association was more robust in those with chronic headaches as compared with episodic headaches. • There was a significant association of obesity with both episodic and chronic (>15 d/mo) migraines. • The link between obesity and tension-type headache was established in some studies but considered to be controversial in others. • Both obesity and weight gain were associated with increased risk for IIH.
Migraine	1B	Winter et al,[81] 2012	Cohort study	n = 19,162	• Patients with a history of migraine headaches were slightly more likely to become overweight or obese in 12.9 y of follow-up (OR, 1.11), but obese patients did not have an increased chance of getting migraines during the same period (OR, 1.00).
	1C	Chorążka et al,[80] 2014	Case-control	n = 78	• There was a correlation of obesity with the frequency of migraine attacks.
	1C	Santos,[82] 2014	Cohort study	n = 5,105	• Increased BMI, but not abdominal obesity, was associated with migraines in adults.
	1B	Verrotti et al,[84] 2014	Cross-sectional study	n = 112	• Subjects with proven insulin resistance had almost 4 times the odds of having chronic migraine compared with those without insulin resistance.
Abdominal and pelvic pain					
Upper abdominal pain	1B (upper abdominal pain) 2B (other abdominal pain)	Eslick,[85] 2012	Meta-analysis	n = Unspecified 16 Studies	• Upper abdominal pain was significantly associated with increased BMI (OR, 2.65). • No significant associations were found for general abdominal pain or lower abdominal pain. • 1B and 2B because the extraction/review was carried out by only 1 author.
Pelvic pain	1C	Gurian et al,[86] 2014	Cross-sectional study	n = 91	• Increased risk of pelvic pain was associated with obesity.
	1C (for men)	Tiuzikov,[87] 2012	Cross-sectional study	n = 250	• Pelvic pain/chronic prostatitis was strongly associated with obesity.
Dysmenorrhea	2A (for women)	Ju et al,[88] 2014	Systematic review	n = 19,010 15 studies	• No significant associations between pelvic pain in women and obesity.

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TABLE 2. *(Continued)*

Condition	Level of Evidence	Source	Type of Study	Cohort or Sample Size	Comments
Neuropathic pain					
Neuropathic pain in general, diabetic neuropathy	1C	Ohayon et al,[89] 2012	Cross-sectional study	n = 3,011	• Obese were at higher risk for chronic neuropathic pain.
	1C	Miscio et al,[90] 2005	Case-control study	n = 41	• Obese subjects had subclinical impairment of nerve function, represented by significantly altered compound muscle action potential amplitude in some lower-extremity nerves and decreased sensory action potential amplitude and impaired sensory thresholds of all examined nerves.
	1C	Herman et al,[91] 2007	Cross-sectional study	n = 73	• Small-fiber neuropathy was present in the obese even before the development of pain and in those with or without hyperglycemia and hyperinsulinemia.
	1C	van Sloten et al,[92] 2011	Cross-sectional study	n = 100	• After exclusion of all persons who manifested mobility limitations, the impaired functional capacity was related to decreased muscle strength and BMI but not neuropathy itself.
Meralgia paresthetica	1C	Mondelli et al,[93] 2007	Case-control study	n = 520	• The risk of meralgia paresthetica was doubled in obese subjects.
Carpal tunnel syndrome	1C	Stallings et al,[94] 1997	Case-control study	n = 600	• Obesity was a risk factor for median neuropathy.

IIH indicates idiopathic intracranial hypertension; TTH, tension-type headaches.

Leptin is a hormone produced by adipocytes, and leptin mRNA concentrations in fat tissue and serum leptin levels closely correlate with fat mass. The hormone's biologic role is primarily to signal a response to nutritional depletion. Homozygous mutations in the genes encoding leptin result in morbid obesity from childhood, hyperphagia, impaired satiety, aggressive behavior when food is denied, and demanding food soon after eating.[1] Genetic variations of substances produced by the adipose cell (eg, visfatin, leptin, tumor necrosis factor α) and many other proteins and signal molecules likely affect individual responses to physiologic, environmental, and psychological stresses seen in both obesity and pain.[108]

An experimental study of a standardized pain stress challenge paired with allelic variation in the leptin gene showed an association with varying levels of dopamine release in response to the pain stressor.[109] The study proved that leptin regulates neuronal activity in humans by influencing the dopamine neurotransmission experience of pain in addition to its primary metabolic function. This helps to explain how a pain-induced dopaminergic response to 1 of the major regulators of the metabolism, leptin, can be genetically predetermined.[109] The clinical significance of this finding is enormous: dopaminergic function plays a major role in mood, substance use, and eating disorders as well as obesity and pain, which potentially have shared genetic polymorphisms and gene expression. A low-grade aseptic inflammation may serve as a common platform for these interactions.[110]

Metabolic and Inflammation Mechanisms

Adipose cells do not function simply for "fat" storage; they play important roles in homeostasis, reproduction, immunity, and inflammatory processes.[111] Available evidence indicates that obesity, pain, and inflammation are linked through multiple central and peripheral neural mechanisms, primarily via altered levels of cytokines (small signaling peptides) and variety of neurotransmitters and even proteins. One study showed that high concentrations of C-reactive protein, a well-recognized inflammatory mediator, may increase the odds of reporting low-back pain, especially in obese individuals.[112] Results of a study of pelvic pain associated with endometriosis suggested that leptin plays a major role in inflammation in addition to pain regulation and metabolic factors.[113]

The traditional hypothesis that obesity contributes to the progression of OA by increasing the load on weight-bearing joints may be an "oversimplification because obesity is also linked to OA in the hand and finger joints."[114] Further research suggests that excessive food consumption, especially saturated fatty acids, regardless of whether the trigger is genetically predetermined or acquired, produces growth of adipose tissue mass, low-grade systemic inflammation, and insulin and leptin resistance. As a result, leptin concentrations increase, triggering the inflammatory process and changing homeostasis in the articular cartilage, ultimately resulting in degeneration.[115] The suggested specific mechanism is an increase in leptin triggering an increase in production of matrix metalloproteinases, proinflammatory mediators, and nitric oxide in chondrocytes, thereby promoting joint damage.[114,116] The association is supported with clinical evidence of worse pain being significantly associated with high synovial concentrations of visfatin, leptin, and interleukin 6 (IL-6) in patients with hip and knee OA.

Importantly, adipokines are likely involved in treatment response and some other phenomena connecting obesity and pain-related behaviors. For example, morphine administration increases leptin expression, glial activation, and dopamine receptor upregulation in the nucleus accumbens.[117] Furthermore, the morphine-satisfying effect is obstructed in leptin-deficient experimental animals or by neutralizing leptin and IL-1β in the same nucleus without diminishing morphine-induced analgesia. These findings

provide evidence for an interface between opioid analgesia and opioid rewarding and may contribute to the understanding of opioid dependency and hyperalgesia tolerance phenomena.[117,118] Further exploration has shown that some reticular formation receptors routinely involved in pain regulation do not work without leptin.[119] The administration of ibuprofen decreased glial activation with no effect on leptin expression in nucleus accumbens in the experimental setting.[117] These findings suggest that better understating of inflammation can create a platform for further developing the interchangeability of some drugs used for pain, behavioral disorders, and obesity. For example, the cyclooxygenase 2–selective anti-inflammatory drug celecoxib may exhibit antidepressant effects, and some mood stabilizers have anti-inflammatory as well as weight-reducing properties. Of note, even small variations of the cytokine molecule can reverse its physiologic effect. For example, although proinflammatory cytokines of the IL-1 family are important factors for inducing obesity, an IL-1 family member, IL-37, was recently found to decrease obesity-induced inflammation and insulin resistance.[120]

Significant correlations have been found between low-grade inflammation and obesity in children.[121] Substantial weight loss was associated with improved insulin resistance and decreased insulin concentrations; correlated with concentrations of interferon γ, IL-6, IL-8, IL-1β, and tumor necrosis factor α^1; and was associated with improvement of migraine.[83] Shared metabolic pathways are well described between migraine and obesity.[122] Initially, their link was seen as symptom interlay (food cravings, thirst, insomnia, mood instabilities).[123] Later, interconnection of obesity and migraine headaches was demonstrated at the hypothalamic level with functional imaging during migraine episodes.[124] Although detailed review of pathologic mechanisms of an obesity-headache association is beyond the scope of this review, it is important to note that aberrations in orexin, adiponectin, leptin, melanocortin receptor 4, serotonin, and their receptors are well described in both obesity and pain and have wide practical applications. For example, selective activation of 5-hydroxytryptamine receptors with lorcaserin produces a cascade of changes leading to appetite suppression through activation of melanocortin 4 receptors. Lorcaserin is 1 of the 4 medicines approved for treatment of obesity by the US Food and Drug Administration (FDA). Furthermore, pharmacologic inhibition of serotonin uptake is a well-known intervention for mood disorders, headaches, and other pain conditions, especially neuropathic pain.

The exact cause of idiopathic intracranial hypertension, which is highly correlated with obesity, is unknown, but it is believed to be associated with disproportionately slow intracranial cerebrospinal fluid absorption and intracranial venous stasis caused by increased intrathoracic pressure resulting from abdominal adiposity.[79] This condition also may have a neuropathic component.

Shared Mechanism of Obesity and Neuropathic Pain

Obesity dramatically increases the risk of peripheral neuropathy, which can produce intractable pain. Obesity and neuropathy have a variety of shared mechanisms, including inadequate glycemic control, prolonged history of diabetes, hypertriglyceridemia, and nephropathy.[90] Obesity is a known risk factor for the development of diabetic neuropathy[125] and is present in up to 50% of patients with diabetes. In addition to pain and dysesthesias, patients are at increased risk of injuries, burns, and distal ulcers.

The etiologies of other neuropathies associated with obesity, such as carpal tunnel syndrome, are not clear.[25] Experimental evidence showed peripheral pain sensitivity aberrations and central sensitization in obese compared with nonobese subjects, but the relationship remains the subject of debate.[126,127] Recently, mechanical factors were brought to the fore when neuropathic knee pain was explained, in part, by turning the innocuous input from high-threshold mechanoreceptors (Aβ-fibers) into painful sensations during joint load.[39]

Biomechanical and Structural Mechanisms

Mechanical and structural factors remain important mechanisms in the obesity and pain association. Obesity may negatively affect cartilage and bone structure and function via several different mechanisms. Serious postural deviations that affect vertical loading, joint misalignment, and structural abnormalities of the spine and joints worsen ambulation and create muscular deconditioning.[25,29] Patients exhibit antalgic gait, increased thoracolumbar stiffness, postural dysfunction, decreased proprioception, and impairment of abdominal and extensor muscles.[29] One group of investigators showed that the combination of obesity and low-back pain affected gait patterns more than obesity alone, including altered knee and ankle patterns during walking.[128] Obesity was associated with reduced disk height in the lumbar spine and recent pain, suggesting that structural changes contribute to back pain and may, in part, explain the association between obesity and back pain.[129]

Certain types of exercises appear to be less traumatic for obese patients. For example, thorough biomechanical evaluation suggests that slow uphill walking may be appropriate exercise for obese individuals at risk for musculoskeletal pathology or pain.[130] The functional and structural restrictions produced by the extra loading of the locomotor system in patients with increased BMIs resulted in an anomalous biomechanical pattern during locomotor tasks, producing abnormalities in other connective tissue structures (tendons, ligament, fasciae, bursae) and increased frequency of injuries, including fractures.[131,132] Occupational medicine literature has established that obese men are at increased risk of multiple rib fractures, and obese women are at greater risk of fracture in the vertebral column, leg, ankle, and humerus and at lesser risk of wrist, hip, and pelvis fractures.[133]

Environmental Mechanisms

Bacteria, viruses, and fungi are known contributors to many rheumatologic and other painful conditions, such as *Propionibacterium acnes* in degenerative disk disease, OA, and sarcoidosis.[134–136] These associations create opportunities for antibiotic treatment of these conditions.[137] Some bowel inhabitants (microbiota) and some other bacteria have been suggested to play a major role in obesity and systemic inflammatory conditions with a known link to pain.[138] The proposed mechanisms involve worsening insulin resistance in the setting of prediabetes or diabetes, and propagating differentiation of the preadipocyte cell line into mature fat cells.[139] The obesity-associated patterns in gut microbiota inherently impaired neurocognitive behavior in an experimental setting by disturbing intestinal barrier function, increasing circulating endotoxins, and increasing lymphocyte expression of some of the calcium-binding receptors.[140] These patterns increased neuroinflammation and disrupted cerebrovascular homeostasis. This link between bowel dysbiosis and neurologic dysfunction may open opportunities for dietary and/or pharmacologic interventions on gut microbiota to attenuate the neuropsychiatric comorbidities of obesity, including depression and pain.

Behavioral Mechanisms

Although environmental and individual mechanisms of obesity and pain are not completely understood, they are linked to an array of behavioral problems, such overeating, pain catastrophizing, kinesiophobia, and depression.[29] A relatively new concept suggests some groups of people "might be addicted to food by losing control over their ability to regulate food intake."[141] Dysfunction of

dopaminergic, serotoninergic, endocannabinoid, and some other domains in the reward circuitry is reported to contribute to "food addiction by regulating appetite and food preference through central and peripheral mechanisms." [141] Some suggest a degree of overlap between pathologic use of drugs, food, and recreational substances. The clinical intersection of these conditions is elevated impulsivity, accompanied by an inability to control the impulse.[142] Cocaine activates dopaminergic pathways in a fashion that is similar to that related to food, with striatal dopamine (D_2 and D_3) receptors modulating the responses.[143] There are indicators that obese patients with chronic pain have disturbances in similar brain reward system circuits, including "hedonic hunger triggered by physical pain and associated with depression and shame," "emotional or 'binge' eating in response to pain," transformed dietary choices as a reaction to pain, and a perception of functional impairment due to pain or depression amplifying the comorbid conditions and complicating treatment.[33] Food-induced analgesia involves activation of the endogenous opioid system as well and can be inhibited by naltrexone administration,[144] which is currently approved in a combination with the antidepressant bupropion for treatment of obesity.

Behavioral factors also may be related to physiologic and genetic changes. For example, maternal obesity during pregnancy increases the risk for descendants' obesity, and ingestion of highly delicious foods by the mother during pregnancy may affect the development of offspring taste inclinations and modify gene expression within the reward system.[145] Obesity at conception as well as during gestation can program the brain reward system by changing expression levels of μ-opioid and preproenkephalin receptors as well as dopamine transporters.[145] Obesity before pregnancy in this experimental study transformed the hypothalamus and reward circuitry (ventral tegmental area, prefrontal cortex, and nucleus accumbens) in adult and late embryonic brains.

Another potential contributor to the behavioral obesity and pain interlay mechanism that is not commonly discussed in the literature is fear of movement.[29] A typical cascade of events is initial injury leading to chronic pain and reduced physical activity that ends in weight gain.[25] Pain associated with fear of movement in obese patients who have persistent low-back pain correlated with self-reported disability and physical performance.[29,146] This may be 1 of the reasons that standard cognitive-behavioral therapy, which appeared not to specifically address this factor, had worse clinical outcomes among obese compared with nonobese patients with persistent low-back pain.[37]

Social and Cultural Mechanisms

Many have suggested that the rise in obesity prevalence over the last decades is driven primarily by the availability of inexpensive appetizing foods and increased energy intake. On the other end of the scale is the trend in reduced energy spending that is associated with decreased physical activity. Very small deviations in daily energy balance, an excess of less than 10 kcal/d above actual requirements, are enough to produce significant increases in the mean BMI of the population.[1]

An important factor that may warrant closer attention by medical professionals caring for obese patients with chronic pains is the dramatic increase in opioid consumption over the last 3 decades, especially in the United States. Opioids can stimulate overconsumption of both fats and carbohydrates, increasing the risk of obesity.[145] Pain physicians prescribe less opioids than other specialties and have lower fatality rates related to opioids,[147] which could place them in the position of assuming a leadership role in collaborating with primary care and specialty colleagues to spur use of alternatives to opioids for long-term treatment of persistent noncancer pain in obese patients.

Implications for Pain Medicine Practice

The Importance of Addressing Obesity in Patients With Chronic Pain

As outlined previously, obesity decreases functional capacity and reduces HRQL in patients with persistent pain by an array of shared pathways.[29,34,35] Recent studies also suggest that individuals suffering from chronic pain and obesity demonstrate worse results to pain management.[29,33,34,38]

Would it be reasonable to expect that pathophysiologic treatment approaches, which may include adjustments in diet, physical activity, lifestyle, and overall disease-related behavior as well as other novel combined pain and weight reduction strategies, may be effective treatment approaches? We explore the available evidence on the effectiveness of combined obesity and chronic pain treatment.

Lifestyle Modification, Patient Education, Behavioral Interventions, Physical Activity, and Other Rehabilitation Strategies

Lifestyle modification remains a pivotal tool in the successful rehabilitation of obese patients with a variety of chronic pain conditions. Such interventions include educating patients on the importance of weight loss, diet, behavior, and modifying the level of physical activity. Comprehensive treatment of obesity and pain may include osteopathic manipulative treatment that, when combined with specific exercises, has been shown to be more effective than exercise alone.[29,148] Some studies also suggest that traditional and modified methods of acupuncture can help with weight loss, pain reduction, and improvement in functional performance.[149] Interestingly, electroacupuncture at the lower limbs and abdomen effectively reduced BMI as well as concentrations of serum leptin, resistin, tumor necrosis factor α, and neuropeptide Y while increasing serum adiponectin and cholecystokinin 8 levels and favorably altered the electrical activity of glucose-inhibited neurons in the lateral hypothalamic area in experimental settings.[150] These treatments as well as cognitive-behavioral therapy, goal setting, and development of problem-solving and coping skills are recognized at various levels of evidence as therapeutic strategies for overweight and obese patients.[25,29,33] The same approaches have been proven to provide simultaneous pain relief.[20,29,151]

Fibromyalgia and widespread pain

Weight reduction in obese patients with fibromyalgia led to a major improvement in the HRQL.[21] Depression, sleep quality, and tender point count in obese patients with this difficult-to-treat condition have improved considerably with weight loss. These and other authors suggested that a weight reduction program should be a standard part of the treatment protocol for obese individuals with fibromyalgia.[21,37] Other researchers suggested that pain management intervention should precede the participation of obese individuals in weight reduction programs.[152]

Headaches

Obesity is considered a modifiable risk factor for migraine headache progression, but whether weight reduction can produce a decrease in headache frequency is unclear. Although obesity is not a proven factor in successful migraine treatment, some have hypothesized that weight loss could be a feasible approach for alleviating headaches in obese individuals.[83,153] A recent systematic review suggested that "clinicians should have a special interest for weight reduction" of obese patients with migraines.[154]

Upper and lower-extremity pain

Numerous systematic reviews and high-quality RCTs in patients with OA have documented the benefit of physical rehabilitation

on both weight loss and OA status. One well-performed study suggested that a modest reduction in weight through diet and exercise resulted in greater improvements in pain and physical performance in obese and overweight patients with knee OA compared with gains with either treatment alone.[155] Aquatic therapy had an advantage over land exercises in obese patients, probably because it was less uncomfortable.[156] The diet + exercise and diet groups had greater weight reduction and greater reductions in IL-6 concentrations than those in the exercise group.[157] Another RCT demonstrated that simple advice on dieting, repeated a few times a year, worked well for both pain control and weight reduction.[158] A diet consisting of 810 kcal/d produced a similar clinical result in obese patients with knee pain as a very-low-energy diet of 415 kcal/d.[159]

Comprehensive treatment of chronic knee pain due to OA was most effective with weight reduction according to 1 systematic review.[160] Dietary intervention plus strengthening exercises seems to be both clinically effective and cost-effective for individuals with knee pain.[161–163] Interestingly, the extent of actual joint damage detected with imaging studies did not affect symptomatic relief following weight reduction.[164]

Advice on lifestyle resulted in weight loss and improved physical fitness in patients with knee pain.[165] French investigators confirmed that physicians should routinely offer structured advice.[166] Advising overweight and obese patients on pain-coping skills and weight management simultaneously seem to provide long-term benefits.[29,38]

Low-back pain

Surprisingly, despite numerous reports of the benefit of weight reduction on OA-associated pain and a significant association of obesity and low-back pain, weight reduction strategies have not been successful in obese patients with low-back pain.[167] Another recently published study showed that a physical rehabilitation program was effective independently of BMI status in patients with persistent low-back pain.[168]Obese patients had overall worse outcomes from both surgical and nonoperative management of lumbar disk herniation.[169] One Korean study showed that obesity did not affect surgical outcomes following lumbar microdiscectomy.[170] In at least 1 study, investigators suggested this may be due to patient noncompliance.[31]

These studies highlight a need for a better understanding of the available treatment options and the development of new approaches to the simultaneous treatment of obesity and pain, such as with pharmacologic options.

Pharmacotherapy for Obesity

Many obese patients cannot lose sufficient weight even with lifestyle and diet modifications.[171] The search for medications to treat obesity has more than a century of history. Amphetamine addiction related to weight reduction stimulated the search for similar drugs without addictive properties.[172] Four sympathomimetic drugs (benzphetamine, diethylpropion, phendimetrazine, and phentermine) are currently approved by the FDA only for short-term (<3 months) use.[173] Phentermine/topiramate is a combination that was approved by the FDA in an extended-release form.[174] The oldest medication available for the long-term treatment of obesity is orlistat, which inhibits gastric and pancreatic lipases after binding to them and decreases absorption of dietary fat through the intestinal mucosa. The drug is excreted through the gut with only 3% systemic absorption.[175] Lorcaserin is a selective 5-hydroxytryptamine receptor agonist that recently received FDA approval for treatment of obesity. Activation of these receptors leads to release of an α-melanocyte–stimulating hormone by the proopiomelanocortin-producing neurons, where these receptors are found in abundance. This hormone, in turn, activates melanocortin 4 receptors, which directly affect appetite suppression.[175] The most recently FDA-approved drug is a combination of naltrexone and bupropion extended-release tablets.[171]

According to a recent systematic review, up to 50% of patients taking lorcaserin and about 70% of patients taking either orlistat or phentermine plus topiramate extended release were able to achieve a more than 5% weight loss over a 1-year period.[176] The naltrexone and bupropion extended-release tablets resulted in an average weight loss of 2% to 4% more than the treatment with placebo over 1 year[177] Of note, the "placebo" included nutrition and physical activity interventions.

Although typical antiobesity drugs are reported to be cost-effective,[178] they are generally expensive and not covered by the government and some commercial insurance companies. In addition, the weight loss is modest, and physicians and patients are wary about their safety because of problems with previous weight loss drugs.[179] All 4 approved medications showed positive effects on metabolism, but no obesity medication has been shown to reduce cardiovascular morbidity or mortality yet,[176] and to the best of our knowledge, no published studies have analyzed their effect on chronic pain.

Pharmacotherapy for Pain in Obese Patients

The differences in pharmacokinetics, pharmacodynamics, and pharmacogenetics between obese and normal-weight subjects are widely discussed in the literature. The deviations triggered by obesity are common and may be initially undetected but ultimately dangerous.[180] Excessive body fat mass can modify the distribution of drugs, especially lipophilic medications. Obese patients have greater muscle mass and increased blood and plasma volumes compared with normal-weight subjects. They also have increased lean body mass; increased cardiac output; decreased pulmonary function; increased proteins and free fatty acids; increased renal blood flow, glomerular filtration rate, and albumin excretion rates; and high levels of hyperfiltration that potentially could result in obesity-related renal failure, nephrotic syndrome, and hypertension.[181]

These physiologic shifts may modify different pharmacokinetic parameters. The increase in plasma blood volumes as well as in fat and muscle mass may alter the distribution volumes of many drugs, with resulting changes in their pharmacodynamics.[180] Obese patients typically have abnormal liver function, accompanied by disarrays in enzymes involved in drug metabolism, resulting in changes in the clinical efficacy of drugs. Overall, the pharmacokinetic alterations observed in obese patients depend on the degree of lipophilicity of the medication and the pathway by which it is metabolized.[181]

Physiologic and pathophysiologic changes associated with obesity are expected to affect drug distribution, binding, and elimination markedly.[180] Prediction of the change in drug metabolism in a specific clinical setting, however, is theoretical. For example, because morphine is expected to be metabolized faster in obese patients, the increased morphine clearance should result in suboptimal pain control compared with normal-weight individuals receiving the same dose. However, BMI did not influence the positive analgesic response to a 4-mg fixed dose of morphine administered to morbidly obese, obese, overweight, and normal-weight individuals in the emergency department setting.[182] Similarly, frovatriptan, in contrast to other triptans, retained a sustained antimigraine effect on obese subjects, possibly because of its longer half-life.[183]

Chronic pain pharmacotherapy should address the concerns of obese patients about iatrogenic weight gain associated with some commonly used pain medications, such as gabapentin or pregabalin. One study showed that about 80% of patients taking 150 to 600 mg/d pregabalin for 1 year maintained their weight within 7% of baseline, but the remainder experienced more

than 7% weight gain, and no one had weight loss.[184] Additional weight gain can promote noncompliance with the therapeutic plan and exacerbation of obesity-related conditions,[185] which may include pain.

The unwanted weight gain may be a reason to support the extension of indications for some drugs in the realm of pain medicine and limit the use of other medicines while the pathway between obesity and pain is further explored. For example, because obesity and addiction share some common physiologic pathways, long-term opioid therapy has the potential for dependency and addiction problems. Topiramate, on the other hand, which is currently approved for migraine prevention, may avert compulsive eating in obese patients, which is one reason that it is currently approved for the treatment of obesity as a part of the previously discussed combination.[174] Some membrane stabilizers, such as zonisamide, may facilitate weight loss.[186]

Morbidly obese individuals commonly take multiple medicines for diabetes, cardiovascular conditions, depression, and other conditions, and such polypharmacy can have untoward effects. Using medications that are approved for a variety of indications may decrease the number of medications taken by patients and potentially decrease the probability of adverse events and unfavorable drug interactions. For example, duloxetine is approved for treatment of depression, generalized anxiety disorder, fibromyalgia, chronic musculoskeletal pain (including OA and low-back pain), and diabetic peripheral neuropathic pain, many of which commonly coexist in morbidly obese patients. The effects of single and combination drugs in obese patients with chronic pain are underexplored and should be researched further.

Morbidly obese patients with chronic pain have high incidence of obstructive sleep apnea, placing them at additional risk of an opioid-induced airway obstruction and hypercapnic respiratory failure with necessary escalation of the opioid dose during chronic use. Furthermore, chronic opioid use is often challenging in morbidly obese patients because of the development of inevitable tolerance to this class of medicine with escalating doses.

Long-term use of opioids, especially in high doses, for obese patients who have noncancer pain should probably be discouraged because of "unproven efficacy and neglected safety."[187]

The benefits of small doses of painkillers before physical therapy or home exercises among obese patients taking opioids represent an important area of further study. The primary barriers to effective physical rehabilitation are usually a poor tolerance of effort, a perception of a low exercise capacity, and a lack of motivation related to the pain associated with physical activity.[188] Another approach to relieving pain associated with physical therapy is to address specific pain concerns with pain management interventions.

Interventional Pain Management in Obese Patients

Despite recent criticism of epidural injection, it remains one of safest and most effective methods of treating acute radicular pain, which is common in obese individuals. However, special considerations are required for obese individuals. The depth of the epidural space differs in obese patients compared with individuals with normal weight.[189] The imaging technique for interventional procedures should be chosen to ensure adequate imaging during the procedure because obesity creates challenges for seeing the target structure. For example, the success rate for lumbar facet injection was significantly lower in obese patients compared with normal-weight patients when ultrasonography was used for needle guidance.[190,191] Some pain blocks, such as of the sciatic nerve in the gluteal area, can be performed faster with modifications to access the targeted structure better in obese patients.[192]

Obese patients are at risk for epidural lipomatosis from epidural injections.[193] Increased adipose tissue can distort the thecal sac and compress neural structures exiting the spinal cord. A review of 70 cases of epidural lipomatosis on magnetic resonance imaging and 34 randomly selected controls showed that the BMI was significantly elevated for the study group and revealed a strong correlation between the number of subsequent epidural corticosteroid injections and new occurrences of epidural lipomatosis.[194] Not only may epidural lipomatosis more likely be present in obese patients than in patients with normal BMIs, but also epidural injections seem to increase the occurrence of epidural lipomatosis in such patients. Existing epidural lipomatosis also can create technical difficulties during other pain management interventions, such as causing high impedance during a spinal cord stimulator trial.[195]

Incautious use of corticosteroids can compromise safety, especially among obese patients who commonly present with impaired glucose metabolism and a history of significant weight gain from previous corticosteroid use.

Other promising treatment strategies are being developed. Platelet-rich plasma (PRP) is a blood derivative with high concentrations of platelets that has been found to have high levels of autologous growth factors, such as transforming growth factor β, platelet-derived growth factor, fibroblastic growth factor, vascular endothelial growth factor, and epidermal growth factor. The PRP can stimulate tissue healing via control of fibrosis and angiogenesis. There are reports of successful use of regenerative medicine technologies, specifically PRP therapy, in the treatment of musculoskeletal pain in obese patients.[196]

Obesity also can shift the homeostatic balance to a predominantly catabolic metabolic process that is linked to pain originating in intervertebral disks. New biologic treatments, gene therapy, and stem cell therapies are being developed,[197] which require the skills of pain medicine physicians to deliver the treatment agents into the disks. Extremely low-frequency magnetic fields have been found to have the ability to inhibit adipogenesis of human mesenchymal stem cells,[198] which may generate a new direction for stem cell therapies. We predict that regenerative medicine tools, including PRP and mesenchymal-derived stem cells, soon will replace many corticosteroid injections.

Remarkably, neuromodulation technology, used to treat chronic pain, has been extended to the treatment of obesity as a target disease.[199]

Interventional Treatment of Obesity

A randomized, double-blind, multicenter, placebo-controlled clinical trial involving 239 morbidly obese patients showed that intermittent vagal nerve blockade was safe and statistically more effective (24.4% excess weight loss vs 15.9% excess weight loss) than a sham procedure.[200] However, the weight loss did not reach the initially set level of clinical significance.

Because deep brain stimulation is considered too invasive for treatment of obesity,[199] a less invasive technique has been developed. C1–C2 neurostimulation can optimize the function of some autonomic nervous structures, possibly related to their proximity to the brainstem, reticular formation, cervical nerve roots containing vagal nerve fibers, and association with the hypothalamus and brain areas regulating homeostasis. The average body mass of morbidly obese patients decreased 5.6 to 8.7 kg in 4 and 8 weeks, respectively, with such neuromodulation, and body fat decreased an average of 7.9 kg in 2 months.[201]

Chronic Pain Management Considerations After Bariatric Surgery

Currently, bariatric surgery is considered the only available treatment with a proven mortality benefit, but only for morbid obesity.[202] In addition, reports suggest the possibility of a noticeable

reduction in both frequency and intensity of hip, knee, and ankle pain as well as the frequency of migraines after bariatric surgery.[203,204] Some reports register no effect of bariatric surgery on pain. Some suggest that bariatric surgery may improve or not change the HRQL.[205,206] The mechanisms of positive or negative clinical outcomes of restrictive bariatric procedures or malabsorptive procedures are still not completely understood,[206] which may explain why the number of long-term complications of surgery remains significant. Pain medicine physicians should be able recognize and manage such complications. Changes in drug absorption after bariatric surgery as well as evolving hormonal alterations must be considered.[207,208] An integrated approach, including collaborative multidisciplinary care that modifies surgical methods and uses additional pain management tools, can decrease the requirement for opioids and encourage rehabilitation.[181,209,210]

Concerning reports indicate that some patients (13%) suffer from worsened depression after bariatric surgery.[211] Another worrisome finding was that despite positive weight-loss outcomes, 77% of patients who were chronic opioid users before bariatric surgery continued such use after surgery, and "the amount of chronic opioid use was greater postoperatively than preoperatively."[212] A factor strongly associated with chronic opioid use postsurgery was presurgery opioid total days' supply of nonnarcotic analgesics, antianxiety medications, and tobacco. Factors associated with a decreased likelihood of chronic opioid use after bariatric surgery included older age and a laparoscopic band procedure (OR, 0.42 vs laparoscopic bypass).[213] The authors suggested the need for developing better pain management in patients following bariatric surgery.

Another clinical study of 30 obese patients before and 7 to 15 days and 6 months after surgery had substantially different findings.[214] The researchers found that Roux-en-Y gastric bypass and subsequent weight loss radically increased the rate of morphine absorption and also somewhat increased morphine exposure. They suggested that the dose of immediate-release forms of morphine might be divided in obese patients after bypass to prevent adverse events due to early and high morphine plasma peaks.

Other common neurologic and hematologic complications of bariatric surgery are typically related to nutritional deficiencies, the most frequent of which are vitamin B_{12}, vitamin D, folate, vitamin E, and thiamine.[215] The pattern of neurologic injury can vary, but commonly results in chronic pain. Peripheral neuropathy, polyradiculopathy, and encephalopathy may be observed early after surgery. Optic neuropathy, myelopathy, myopathy, and late peripheral neuropathy may develop many years after the procedure. Accordingly, patients should be monitored routinely at 6 weeks and 3, 6, and 12 months after the surgery and offered yearly monitoring, including laboratory studies and multivitamin supplementation.[215]

Monitoring the Effect of Chronic Pain and Obesity Treatment

Routine BMI monitoring is an important tool in combined management of obesity and pain. Routine chronic pain assessment scales alone, however, are not sufficient to monitor progress of pain primarily because the major outcome measure in patients in rehabilitation is functional status and HRQL. Self-report questionnaires of pain-related disability, rather than only pain scores, are more likely to provide an accurate illustration of a patient's level of ability at the time of assessment.[216] Many obese patients are inactive due to pain, which creates a vicious cycle. Accelerometry was effective in a study monitoring relationships among obesity, chronic pain, and mobility. This approach might be extended to routine practice because the device is readily available on the "smartest" phones.[58] Because BMI was found to be the dominant predictor of physical function in patients with lumbar spinal stenosis, researchers suggested implementation of "e-health lifestyle intervention" aimed at reducing BMI and improving functional status of these patients.[217] The key components of this treatment protocol include pedometer-based physical activity promotion and diet education.

Mobile applications and their Web counterparts may promote physical activity.[218] A recent systematic review of the evidence of mobile phone use for weight reduction identified 43 studies of obese or overweight subjects showing that patient engagement in the program was the best predictor of positive outcome.[219] These applications, along with mobile fat composition measuring tools, may serve as a convenient platform for monitoring both patient and physician performance.

Remote management of pain pumps by physicians for continuous peripheral nerve blocks based on patient feedback is available[220] and can be potentially adapted for application in obese patients with chronic pain. Mobile device short message service and relevant applications have been effectively used in a management weight loss program in China.[221] Because of the wide penetration of mobile devices in developed countries, these approaches have the potential for effective management of compliance with the therapeutic plan in obese patients with chronic pain.

Infrastructure for Treatment of Obesity Within Pain Medicine

Most available evidence supports the concept that weight reduction helps to alleviate chronic pain, improve HRQL, and diminish the effects of pain-related disability.[222] However, inadequate pain control is a major barrier to effective implementation of these programs. The pain complaints and comorbidities of obese patients who have chronic pain can challenge the scope of practice of any single medical specialty. Therefore, effective communication with colleagues, extension of skills, and increased depth of knowledge are fundamental for pain physicians to provide effective help for these complex patients.[21,223] One expert review suggested that incorporation of weight reduction treatment into the routine pain management of patients with increased BMIs could "represent what the Institute of Medicine calls a 'cultural transformation' in our understanding of pain states and our approach to the clinical encounter."[103]

The first step in this direction is BMI calculation for each patient with chronic pain. Such calculation should become a routine part of screening assessment for patients with persistent pain, with additional screening for pain- and obesity-related disability and behavioral disarrays in obese patients.[33,34]

The next step is to design a treatment strategy based on individual patient characteristics. Surgical treatment, which is beyond the scope of this review, may be indicated for morbidly obese patients, but clinicians should be aware that bariatric surgery presents perioperative challenges and has the potential for numerous complications, even when surgery is considered successful.[215]

Pain medicine physicians can readily adapt conservative rehabilitation strategies because the tools and infrastructure needed for treatment of obesity already exist in the realm of pain medicine. These include patient education and behavioral medicine approaches, physical rehabilitation, medications, and interventional treatment that can be implemented in the pain management office setting.

The next logical step is establishment of effective treatment monitoring systems, which are already routinely used in pain management clinics. These can be upgraded with novel e-health tools discussed.

Additional Training

The simultaneous management of obesity and chronic pain will require additional physician and staff training. Office staff should be educated about the nature of obesity to improve patient satisfaction and treatment outcomes. Without targeted education,

the prevalence of negative attitudes toward obese patients in the rehabilitation office setting can be high, as illustrated by 4% of responders in an anonymous, self-report survey "exhibiting high levels of antifat attitudes."[224] Some studies suggest that physician residents may be uncomfortable managing obesity. Obesity-specific didactic curricula are available[225] and can be modified to fit pain medicine fellowship curricula. Their implementation can improve fellows' familiarity with obesity, outlook about the condition, and practice patterns, potentially improving clinical outcomes in obese patients with chronic pain.

One of the most important aspects of such training is the strong encouragement to collaborate with primary care, endocrinology, and the bariatric team to provide comprehensive and safe care for obese patients. The following illustrates the importance of seeing obese patients with the "eyes" of colleagues of other specialties. Despite obesity facilitating the development of cancer and cardiometabolic diseases, it may have protective effect on mortality once these conditions occur.[226] Active weight loss of 7.5% and more of body weight was a robust predictor of decreased survival of patients with persistent coronary vascular disease complicated by diabetes, whereas weight gain was not associated with increased mortality. Therefore, consulting with primary care, cardiologists, oncologists, and other relevant specialists about the initiation of weight reduction programs for a medically complicated patient is very important.[227] The window of opportunity for sick patients appears to be relatively small; at least a 5% weight reduction over 20 weeks or a rate of 0.25% per week is required to improve pain in patients with knee OA according to a systematic review of 35 eligible RCTs.[228]

CONCLUSIONS

The combination of obesity and chronic pain is extremely prevalent. Effective treatment of pain in obese patients remains very challenging for a variety of reasons, but primarily because of a lack of tools and infrastructure to "address the symbiotic relationship between the 2 conditions."[33]

However, when applied appropriately and comprehensively, weight reduction can help to alleviate pain related to obesity, improve HRQL, and diminish the effects of pain-related disability. Because obese patients frequently present with a set of pain complaints and comorbidities that challenge the scope of practice of any single medical specialty, pain physicians must extend their skills and depth of knowledge to provide comprehensive care for these complex patients. Fortunately, the tools and infrastructure needed for treatment of obesity already exist in the realm of pain medicine (patient education and behavioral medicine approaches, physical rehabilitation, medications, and interventional treatment). Assessing BMI, screening for pain-obesity related disability, evaluation for behavioral disarrays, and monitoring of functional performance should become a routine part of pain medicine practice. The combined management of chronic pain and obesity in patients who can benefit from this strategy will likely require extensive office staff and physician training. Specific pain management protocols must be developed for patients who are undergoing bariatric surgery because of the risk of remote complications. Development of new technologies to help patients with pain and obesity, including neuromodulation approaches, mobile technologies, e-health, and other tools, as well as further exploration of the nature and strength of the associations between obesity and chronic pain, can provide a better understanding of the interplay between these 2 very common conditions.

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